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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/523,279	JONES ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner for this application currently pending at the USPTO has changed.

Examiner Samira Jean-Louis can be reached at 571-270-3503.

Response to Amendment

This Office Action is in response to the amendment submitted on 01/17/2008. Claims 1-7 and 12-15 are pending in the applications, with claims 8-11 having being cancelled. Accordingly, claims 1-7 and 12-15 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

Examiner further acknowledges amendment of claim 12 and consequently the objection to claim 12 has been withdrawn. However, due to the alpha-adrenoceptor antagonist abanoquil occurring twice in claim 4, the objection to claim 4 is still maintained.

Applicant's arguments that Wyllie does not suggest any teaching or suggestion that the muscarinic antagonist can be substituted with any of the 5 HT-4 modulators of Sanger to yield a composition useful for the treatment of lower urinary tract symptoms has been considered but is not persuasive. It is respectfully pointed to applicant that the rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, or it may be drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would

have been produced by their combination (see *In re Semaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). See also Dystar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick, 464 F.3d 1356, 1368, 80 USPQ2d 1641, 1651 (Fed. Cir. 2006). Consequently, because the muscarinic receptor antagonists could potentially lead to unpleasant side effects (i.e. dry mouth, dry eyes, etc...), one of ordinary skill in the art, would have been motivated to substitute the 5 HT4 receptor antagonists of Sanger in lieu of the muscarinic receptor in order to reduce unwanted side effects. In fact, studies performed by Matsui et al. demonstrated that the muscarinic receptor plays a vital role in salivary secretion, papillary constriction and bladder detrusor contractions (Matsui et al., see abstract, pg. 9579). Moreover, loss of the muscarinic receptor lead to attenuated salivary responses and weak papillary contractions (Matsui et al. see pg. 9583). Thus, to one of ordinary skill in the art at the time of the invention would have been motivated to substitute the 5 HT-4 receptor antagonist for the muscarinic receptor in order to avoid the unwanted side effects induced by inhibiting or suppressing the muscarinic receptors.

Applicant's contention that it is inappropriate for the Examiner to take official notice of facts without citing a prior art reference where the facts asserted to be well known has been considered but is not persuasive. The fact that muscarinic receptor inhibition or suppression leads to undesired side effects is well known in the art. Again, Examiner refers applicant to the statement above which delineates that loss of muscarinic receptors as evidenced by Matsui et al. does indeed lead to attenuation of

salivary responses and pupillary contractions. Thus, Matsui et al. is being provided as evidentiary support of the well-known fact that loss or inhibition of muscarinic receptors can and do lead to certain unwanted side effects (see Matsui et al. PNAS Vol. 97, No. 17, pgs. 9579-9584).

Applicant's argument that substitution of a 5 HT-4 antagonist for the muscarinic antagonist would not have produced a predictable, successful result has been considered but is not found persuasive. Willie et al. teaches the combinatorial use of alpha adrenergic receptor antagonists and muscarinic receptor antagonist for the treatment of lower urinary tract symptoms associated with BPH in mammals; Sanger, on the other hand, teaches the use of 5 HT-4 receptor antagonists for urinary incontinence including overactive bladder, thus it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the two compositions since they both teach their composition as effective against urinary incontinence. Thus, one of ordinary skill would have been motivated to combine the two compositions given that the two compositions are useful for the same purpose and one of ordinary skill would have the reasonable expectation of obtaining a composition that is successful in treating lower urinary tract symptoms. Examiner further notes that as a general principle it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining them flows logically from their having been individually taught in the prior art. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ

1069, 1072 (CCPA 1980) **MPEP 2144.06.** Regardless of the type of compositions argued in *In re Kerkhoven*, it would have been obvious to one of ordinary skill to combine any two compositions taught by the prior art for the same purpose with a reasonable expectation of success.

For the foregoing reasons, rejection of claims 1-7 and 12-15 under 103 (a) remains proper and is maintained. However, in view of applicant's amendment, the following 112, 1rst paragraph, 102 (b) and modified 103 (a) Non-Final rejections are being made.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In this application, the particular combination of an alpha adrenoceptor antagonist such as abanoquil with a 5 HT-4 antagonist such as SB 205800 is critical or essential to the practice of the invention, however, applicant did not specifically described the particular combinations of alpha-

adrenoceptor antagonists with 5 HT-4 receptor antagonists in the claim(s) (i.e. claims 1 and 13-15) or in the specification (see specification pg. 9, lines 15-24, and pg. 6, lines 18-24). Consequently, due to this lack of written description, the exact alpha adrenoceptor antagonists and 5 HT-4 receptor antagonists being claimed by applicant to be used in their method cannot be fully ascertained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-6 and 12 are rejected under 35 U.S.C. 102(a) as being anticipated by Radulovacki et al. (U.S. 6,331,536 B1).

It is respectfully pointed out that the intended use for the composition has not been given patentable weight because the invention is directed to a composition in claims 1-6. An intended use is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535

F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robbie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Specifically, Radulovacki et al. teaches the combination of serotonin receptor antagonists in conjunction with an alpha 2 adrenergic receptor for the prevention of sleep related breathing disorders (see col. 4, lines 65-67 and col. 5, lines 1-2). Example of serotonin includes the 5HT-4 receptor antagonist SDZ-205, 557 and examples of alpha adrenergic receptors antagonists include terazosin, doxazosin, indoramin and prazosin (see col. 5, lines 20-21, 24, and 36-39). The administration of the combination of the serotonin receptor antagonist (i.e. 5HT-4 receptor antagonist) with the alpha 2 adrenergic receptor antagonist may be involved the any systemic means including intravenous or intramuscular or intraperitoneal (see col. 5, lines 6-8). As for the inclusion of a carrier, it is concluded that Radulovacki et al. teaches the carrier inherently as the compounds are solids and Radulovacki et al. teaches the composition for intravenous administration. As a result, Radulovacki et al. inherently teaches the carrier in the aforementioned combination since the composition is being administered intravenously (i.e. containing a vehicle carrier).

Accordingly, the teachings of Radulovacki et al. anticipate claims 1-6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 and 12-15 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Wyllie (U.S. 7,138,405, previously cited) in view of Sanger et al. (U.S. 2002/0128172, previously cited).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Wyllie teaches pharmaceutical combinations of alpha-adrenoceptor antagonist and muscarinic antagonist suitable for the treatment of lower urinary track symptoms including benign prostatic hyperplasia (BPH) that may be administered simultaneously,

separately or sequentially (instant claims 13 and 15; see abstract and summary of invention, lines 1-17). Wyllie further teaches that bladder excitability can lead to unstable bladder contractions (i.e. overactive bladder; instant claim 14; see col. 2, lines 35-45). Suitable alpha adrenoceptor antagonists include both selective and non selective (instant claims 2-3) antagonists and preferably include alfuzosin, indoramin, tasulosin, doxazosin, terazosin, abanoquil, and prazosin (see col. 3, lines 45-50 and 56-65). The aforementioned compounds can be administered as an admixture with a suitable pharmaceutical excipient, diluent or carrier (instant claim 1; see col. 7, lines 15-19).

Wyllie et al. does not particularly teach a method of treating lower urinary track symptoms containing both an alpha adrenoceptor antagonist and a 5-HT4 receptor.

Sanger et al. teaches the use of 5 HT-4 receptors for the treatment associated with urinary incontinence or bladder hypersensitivity (i.e. overactive bladder; instant claim 14; see abstract and pg. 1, paragraph 00006 and pg. 2, claims 1-4). Suitable 5-HT4 receptor antagonists include SDZ 205-557, R 50595, DAU 6285, and RS 23597-190 (instant claims 5-6; see pg. 1, paragraph 0009 and pg. 2, claim 7) which are administered with a suitable carrier (instant claim 1; see pg. 2, paragraph 0027).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to combine the method of Wyllie with the method of Sanger et al. since

both teach a method of treating lower urinary track symptoms. Given that Wyllie teaches pharmaceutical combinations of alpha-adrenoceptor antagonist and muscarinic antagonist suitable for the treatment of lower urinary track symptoms including benign prostatic hyperplasia, and Sanger et al. teaches the use of 5 HT-4 receptors for the treatment associated with urinary incontinence or bladder hypersensitivity, one of ordinary skill would have been motivated to combine the method of Wyllie and that of Sanger et al. with the reasonable expectation of providing an enhanced method that is efficacious in treating lower urinary tract symptoms including overactive bladder and BPH.

Moreover, it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose, the idea of combining them flows logically from their having been individually taught in the prior art. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06.**

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wyllie (U.S. 7,138,405, previously cited) in view of Sanger et al. (U.S. 2002/0128172, previously cited) as applied to claims 1-6 and 12-15 above and in further view of Bosmans et al. (WO 00/037461).

The Wyllie and Sanger references are as discussed above and incorporated by reference herein. However, Wyllie and Sanger do not address the particular 5-HT4

antagonist (3S-trans)-4-(4-[[(8-chloro-3,4-dihydro-2H benzo[b] [1,4]dioxepine-6-carbonyl)-amino]-methyl]-3-hydroxy-piperidin-1-yl)-butyric acid as the 5 HT-4 antagonist in the composition for treating lower urinary track symptoms.

Bosmans et al. teaches compounds with potent 5 HT-4 antagonistic activities (see pg. 18, lines 28-34). Bosmans et al. further teaches that his compounds that possess 5-HT-4 antagonistic activity include (3S-trans)-4-(4-[[(8-chloro-3,4-dihydro-2H benzo[b] [1,4]dioxepine-6- carbonyl)-amino]-methyl]-3-hydroxy-piperidin-1-yl)-butyric acid which is a 5-HT-4 antagonist (instant claim 7, see pg. 43, compound 156).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to combine the method of Wyllie with the method of Sanger et al. and substitute the 5-HT4 antagonist since both Wyllie and Sanger et al. teach a method of treating lower urinary track symptoms and Bosmans et al. teaches compounds possessing 5-HT-4 antagonistic activities. Moreover, it is considered that one of ordinary skill in the art at the time of the invention was made would have found it obvious to substitute 5-HT-4 antagonistic activity including (3S-trans)-4-(4-[[(8-chloro-3,4-dihydro-2H benzo[b] [1,4]dioxepine-6- carbonyl)-amino]-methyl]-3-hydroxy-piperidin-1-yl)-butyric acid of Bosmans et al. for the 5-HT-4 antagonist of Saner et al. given that the substitution of one known element for another would have yielded predictable results.

Given that Wyllie teaches pharmaceutical combinations of alpha-adrenoceptor antagonist and muscarinic antagonist suitable for the treatment of lower urinary track symptoms including benign prostatic hyperplasia, and Sanger et al. teaches the use of 5 HT-4 receptors for the treatment associated with urinary incontinence or bladder hypersensitivity, and Bosmans et al. teaches 5-HT-4 antagonists, one of ordinary skill would have been motivated to combine the method of Wyllie and that of Sanger et al. and substitute the compound of Bosmans et al. into the methods of Wyllie and Sanger with the reasonable expectation of providing an enhanced method that is efficacious in treating lower urinary tract symptoms including overactive bladder and BPH.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

04/21/2008

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617